AMENDMENT – Claims

Please amend claim 3 as follows:

1. (previously presented) A method for delivering a therapeutic agent to a subject, comprising;

introducing an effective amount of at least one therapeutic agent into a target muscle tissue site of a subject, wherein the therapeutic agent comprises a polynucleotide that encodes a therapeutic protein or peptide; and

generating an electric field at the target muscle tissue site by introducing from 1 to about 4 monopolar DC pulses, each pulse having a duration of about 10 ms to about 100 ms, to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle tissue site.

2. (previously presented) A method according to claim 1, that reduces histopathological change at the target muscle tissue site as a result of the application of the electric field.

3. (currently amended) A method according to claim 2 ~~3~~, wherein the histopathological change is selected from the group consisting of inflammation, induction or amplification of an immune response, necrosis, and fibrosis.

4-5. (canceled)

6. (previously presented) A method according to claim 1, wherein the duration of each pulse is in the range from about 20 ms to about 60 ms.

7. (previously presented) A method according to claim 1, wherein there are no more than two pulses at each target muscle tissue site.

8. (previously presented) A method according to claim 1, wherein the nominal field strength is in the range from about 100V/cm to about 232V/cm.

9. (previously presented) A method according to claim 8, wherein the nominal field strength is in the range from about 100V/cm to about 150V/cm.

10. (previously presented) A method according to claim 8, wherein the duration of each pulse is in the range from about 40 ms to about 60 ms.

11. (currently amended) A method according to claim 1, wherein the electric field is generated by applying electroporation electrodes to the subject, wherein a portion of the electrodes that contact[[s]] the subject is made of a non-toxic, biocompatible metal.

12. (previously presented) A method according to claim 11, wherein the metal is gold.

13. (previously presented) A method according to claim 1, wherein the subject is a mammal.

14. (previously presented) A method according to claim 1, wherein the subject is a human.

15. (previously presented) An *in vivo* method for expressing a therapeutic polypeptide or peptide encoded by an isolated polynucleotide delivered into cells in a subject, comprising;

a) introducing at least one isolated polynucleotide encoding a therapeutic polypeptide or peptide into a target muscle tissue site of a subject; and

b) generating an electric field at the target muscle tissue site by introducing from 1 to about 4 monopolar DC pulses, each having a pulse duration of about 10 to about 100 ms, to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle tissue site.

16. (previously presented) A method according to claim 15 that reduces histopathological change at the target muscle tissue site as a result of the application of the electric field.

17. (previously presented) A method according to claim 16, wherein the histopathological change is selected from the group consisting of inflammation, induction or amplification of an immune response, necrosis, and fibrosis.

18. (previously presented) A method according to claim 15, wherein the duration is in the range selected from the group consisting of from about 20 ms to about 60 ms and from about 40 ms to about 60 ms.

19. (previously presented) A method according to claim 15, wherein there are no more than two pulses.

20. (previously presented) A method according to claim 15, wherein the nominal field strength is in the range from about 100V to about 150V.

21. (previously presented) A method according to claim 15, wherein the polynucleotide is introduced at substantially the same time as generating the electric field.

22. (currently amended) A method according to claim 15, wherein the electric field is generated by applying to the subject electroporation electrodes, wherein a portion of the electrodes that contact[[s]] the subject is made of a non-toxic, biocompatible metal.

23. (previously presented) A method according to claim 22, wherein the metal is gold.

24. (previously presented) A method according to claim 15, wherein the subject is a mammal.

25. (previously presented) A method according to claim 15, wherein the subject is a human.

26. (previously presented) A method according to claim 15, wherein the polynucleotide is injected intramuscularly at from 1 to about 20 sites in the target muscle tissue.

27. (previously presented) A method according to claim 15, wherein said polynucleotide is selected from the group consisting of double stranded DNA, single-stranded DNA, complexed DNA, formulated DNA, encapsulated DNA, naked RNA, encapsulated RNA, and combinations thereof.

28. (previously presented) A method according to claim 15, wherein the polynucleotide encoding the therapeutic polynucleotide is contained in a DNA vector.

29. (previously presented) A method according to claim 15, said polynucleotide being operably associated with a regulatory sequence for expression of the therapeutic polypeptide or peptide in said cells.

30. (previously presented) A method according to claim 15, wherein said polynucleotide further encodes a selectable marker polypeptide.

31. (previously presented) A method according to claim 29, wherein said regulatory sequence comprises a promoter.

32. (previously presented) A method according to claim 31, wherein said promoter is muscle specific.

33. (currently amended) A method according to claim 32, wherein said promoter is a promoter selected from the group consisting of a CMV promoter, a RSV LTR, a MPSV LTR, and a SV40 promoter[[s]].

34. (previously presented) A method according to claim 15, wherein the electric pulses are administered to the target muscle tissue using an electroporation electrode comprising a plurality of electrically conducting needles.

35. (previously presented) A method according to claim 34, wherein a portion of the needles that contacts the subject is made of a non-toxic, biocompatible metal.

36. (previously presented) A method according to claim 35, wherein the metal is gold.

37. (previously presented) A method for delivering a polynucleotide encoding a peptide or polypeptide to a target muscle tissue site, comprising:

a) introducing an effective amount of at least one isolated polynucleotide encoding a peptide or polypeptide into a target muscle tissue site of a subject;
b) introducing at least a conductive portion of an electrode needle array into the target muscle tissue; and
c) c) applying from 1 to about 4 monopolar DC pulses having a duration of about 10 ms to about 100 ms each to generate a nominal field strength of about 100V/cm to about 300V/cm at the target muscle site, thereby delivering the polynucleotide to the target muscle tissue site.

38. (previously presented) A method according to claim 37, wherein the electrode needle array comprises four electrode needles and two pulses are applied to the target muscle tissue site to generate a nominal field strength of about 116 V/cm.